Gamma-secretase cleavage of the p75 receptor

https://neurodegenerationresearch.eu/survey/gamma-secretase-cleavage-of-the-p75-receptor/

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Contact information of lead PI
Country

USA

Title of project or programme

Gamma-secretase cleavage of the p75 receptor

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,513,970.64

Start date of award

01/12/2004

Total duration of award in years

10

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Regenerative Medicine... Stem Cell Research... Stem Cell Research - Induced Pluripotent Stem Cell... Stem Cell Research - Induced Pluripotent Stem Cell - Non-Human

Research Abstract

DESCRIPTION (provided by applicant): Neurotrophins exert trophic and synaptic effects

through the actions of two different receptors, Trk tyrosine kinases and the p75 neurotrophin receptor. In addition to Trk receptor signaling, p75 is cleaved through a process that is very similar to the cleavage of amyloid precursor protein. The hypothesis of this grant is that ?-secretase activity plays a critical role in controlling the signaling repertoire for neurotrophin receptors. Regulated intramembrane proteolysis of the p75 may regulate several important actions of neurotrophins through differential signaling by Trk receptors. Significantly, withdrawal of trophic factors gives rise to a series of events that leads to greater processing of amyloid precursor protein (APP), which may contribute to the selective dysfunction and degeneration of p75-expressing neurons in Alzheimer’s disease. Because of the vulnerability of basal forebrain cholinergic neurons, this proposal will seek to generate basal forebrain neurons in primary culture and also by differentiating induced pluripotent stem cells. Gene expression profiles will be obtained after withdrawal of NGF and BDNF from neuronal cultures. These will allow us to study the fundamental consequences of how loss of trophic support, ?-secretase cleavage of p75, and Trk receptor signaling influence APP metabolism.

Lay Summary
The properties of neurotrophins and their receptors will help to understand their roles during development and in neurodegenerative diseases, such as Parkinson’s and Alzheimer’s diseases and amyotrophic lateral sclerosis. This grant application will focus upon the action of neurotrophins and their receptors, Trk and p75, when there is loss of trophic support. The consequences of ?-secretase cleavage of p75, a receptor that is expressed after nerve damage, inflammation and neurodegeneration, will be followed. A key unexplored question is how deprivation of neurotrophins is related to increases in the processing of amyloid precursor protein. The proposed studies will give further insights into the consequences of ?-secretase cleavage of p75 and how the processing of APP is influenced by trophic factor withdrawal.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A